

Application No.: 09/555,349

IN THE CLAIMS:

1-13. (Canceled)

14. (Withdrawn) A method for production of polyclonal antibodies to an antigen comprising immunizing an animal having antibody-producing cells with disrupted peripheral tolerance with said antigen to permit said antibody-producing cells to produce antibodies to said antigen and separating serum, which contains said polyclonal antibodies, from said animal.

15. (Withdrawn) The method of claim 14, wherein said animal is selected from the group consisting of a mouse, rat, pig, guinea pig, poultry, a goat, a sheep, primate and a rabbit.

16. (Withdrawn) The method of claim 15, wherein said animal is a mouse.

17. (Withdrawn) The method of claim 16, wherein said mouse is a transgenic mouse overexpressing CD19.

18. (Withdrawn) The method of claim 14, wherein said antibody-producing cells comprise B lymphocytes.

19. (Withdrawn) A diagnostic assay kit for detecting the presence of an antigen in a biological sample, the kit comprising a first container containing a first antibody capable of immunoreacting with the antigen, wherein the first antibody is produced from an animal having antibody-producing cells with disrupted peripheral tolerance and the first antibody is present in an amount sufficient to perform at least one assay.

20. (Withdrawn) The assay kit of claim 19, further comprising a second container containing a second antibody that immunoreacts with the first antibody,

Application No.: 09/555,349

wherein second antibody is produced from an animal having antibody-producing cells with disrupted peripheral tolerance.

21. (Withdrawn) The assay kit of claim 20, wherein the first antibody and the second antibody comprise monoclonal antibodies.

22. (Withdrawn) The assay kit of claim 21, wherein said first antibody comprises an antibody having a high affinity for said antigen.

23. (Withdrawn) The assay kit of claim 20, wherein the first antibody is affixed to a solid support.

24. (Withdrawn) The assay kit of claim 20, wherein the first and second antibodies each further comprise an indicator.

25. (Withdrawn) An assay kit of claim 24, wherein the indicator is a radioactive label or an enzyme.

26. (Withdrawn) A method of producing a non-human animal with an immune system having cells with a predetermined characteristic, the method comprising the steps of:

- (a) obtaining an animal having immune system cells with a particular characteristic;
- (b) obtaining another animal having immune system cells with either a same or a different characteristic from the animal of step (a); and
- (c) breeding the animal of step (a) with the animal of step (b) to produce an animal with an immune system having cells with a predetermined characteristic.

Application No.: 09/555,349

27. (Withdrawn) The method of claim 26, wherein said animals are selected from the group consisting of a mouse, rat, pig, guinea pig, poultry, a goat, a sheep, primate and a rabbit.

28. (Withdrawn) The method of claim 27, wherein said animals are transgenic animals.

29. (Currently Amended) A method for producing a monoclonal antibody specific for an antigen, the method comprising:

- (a) immunizing a transgenic mouse overexpressing CD19, and having antibody-producing cells with disrupted peripheral tolerance, with an antigen to permit said antibody-producing cells to produce antibodies to the antigen;
- (b) removing at least a portion of said antibody-producing cells from the mouse;
- (c) forming a hybridoma by fusing one of the antibody-producing cells with an immortalizing cell wherein the hybridoma is capable of producing a monoclonal antibody to the antigen;
- (d) propagating the hybridoma; and
- (e) harvesting the monoclonal antibodies produced by the hybridoma, the monoclonal antibodies having a diverse repertoire of  $V_H$  and  $V_L$  rearrangements.

30. (Previously Presented) The method of claim 29, wherein said monoclonal antibodies comprise antibodies having an affinity constant of greater than  $1 \times 10^5$  liters per mole for said antigen.

31. (New) The method of claim 29, wherein said monoclonal antibodies produced by the hybridoma are characterized by the presence of two (2) or fewer somatic mutations in a  $V_H$  region.

Application No.: 09/555,349

32. (New) A method for producing a monoclonal antibody specific for an antigen, the method comprising:

- (a) immunizing a transgenic mouse overexpressing CD19, and having antibody-producing cells with disrupted peripheral tolerance, with an antigen to permit said antibody-producing cells to produce antibodies to the antigen, wherein said antigen is selected from the group consisting of an autoantigen and a highly conserved antigen;
- (b) removing at least a portion of said antibody-producing cells from the mouse;
- (c) forming a hybridoma by fusing one of the antibody-producing cells with an immortalizing cell wherein the hybridoma is capable of producing a monoclonal antibody to the antigen;
- (d) propagating the hybridoma; and
- (e) harvesting the monoclonal antibodies produced by the hybridoma.